Hyponatraemia - Principles, Investigation and Management

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Biochemistry
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Background

- Relatively common:
  - Estimated 15-30% prevalence in all acute admissions
  - Prevalence 2.48% in community with 0.97% incidence in 1985

- Associated with gait disturbance, cognitive disturbance, osteoporosis and mortality
  - (Not causative)
Background

- **Hyponatraemia**: Serum sodium of less than 135mmol/L
  - Mild: 130-135
  - Moderate: 125-129
  - Severe: <125

- Acute is <48 hours, Chronic is >48 hours.

- Reflects serum osmolality

- Hyponatraemia causes cell overhydration
Background adaptation

- Normal brain (normal osmolality)
  - Immediate effect of hypotonic state
  - Water gain (low osmolality)
  - Rapid adaptation
  - Proper therapy (slow correction of the hypotonic state)
  - Osmotic demyelination
  - Improper therapy (rapid correction of the hypotonic state)
  - Loss of organic osmoles (low osmolality)
    - Loss of sodium, potassium, and chloride (low osmolality)
    - Slow adaptation
    - Water
Background

- **Normal**
  - 1L /1Kg
  - Na 135
  - Osm/Kg-280

- **Pseudo hyponatraemia**
  - 1L
  - Na 125
  - Osm/Kg-280

- **Pseudo hyponatraemia**
  - 1Kg
  - Na 135
  - Osm/Kg-280

- **True hyponatraemia**
  - 1L /1Kg
  - Na 125
  - Osm/Kg-265
Background

Normal fraction of solid-phase particles

Increased fraction of solid-phase particles

Water phase

Solid phase

Standard volume of diluent added
Background - Symptoms

• **Mild:**
  - Asymptomatic
  - Headache, anorexia, nausea, lethargy

• **Moderate:**
  - Confusion, muscle cramps, weakness, confusion, ataxia

• **Severe:**
  - Drowsiness, coma, vomiting, brainstem herniation, seizures

• **Rapid correction:**
  - Cerebral pontine demyelinolysis
Assessment

**Examination**
- Capillary refill
- Tissue turgor
- Radial pulse - ?tachycardia
- Mucous membranes
- JVP
- Heart sound - ?flow murmurs ?S3
- Breath sounds - ?crepitations
- Ascites
- Peripheral oedema

**Investigations**
- U+Es
- LFTs
- Osmolality (paired serum and urine)
- Urine Sodium and Potassium
- Thyroid function Tests
- 9am Cortisol
- CXR
- CT Head (?SIADH)

If required:
- Lipid profile
- Protein electrophoresis
- Glucose
Normal Osmolalities - Pseudohyponatremia

Hyponatraemia

Normal osmolality

Pseudohyponatraemia

Hyperlipidaemia/
Hyperproteinaemia

- High levels of lipid or protein
- Does not contribute to osmolality

Appropriate

Hyperglycaemia

- Compensated osmolality
- Possibly raised osmolar gap depending on cause

Sick Cell Syndrome

- Na/K ATP-ase dysfunction
- Associated with hypoxia and sepsis
- Normal compensated osmolality

Corrected plasma Sodium:

Measured Sodium conc. + Plasma glucose

\[ \frac{\text{Plasma glucose}}{4} \]
Classification

Hyponatraemia

Low osmolality

Hypovolaemic

- Urine Na >30
  - Aldosterone deficiency
  - Dieuretic excess
  - Salt losing nephropathy
  - Cerebral salt wasting

- Urine Na <30
  - Vomiting
  - Burns
  - Diarrhoea
  - Pancreatitis

Euvolaemic

- Urine Na >30
  - SIADH
  - Glucocorticoid deficiency

- Urine Na <30
  - Hypothyroid
  - Water Overload

Hypervolaemic

- Urine Na >30
  - Renal Failure
  - Heart Failure
  - Cirrhosis
  - Nephrotic Syndrome

- Urine Na <30
General Management - Emergencies

- If evidence of brain herniation:
  - Aim to raise Na by 5mmol/L in first hour, and then 1mmol/hr until resolution of neurological symptoms
  - If no resolution: aim to raise sodium to approximately 130mmol/L or by max 10mmol/L
  - Involve ITU
  - Sodium measurements 6 hourly

- Use Hypertonic saline
  - 3% saline in emergencies

- Reduces volume of fluid given
General Management - Emergencies

Within first hour:
- IV infusion 150 mL 3% hypertonic saline or equivalent
- Over 20 min
- Close monitoring environment

Check Na⁺:
- IV infusion 150 mL 3% hypertonic saline or equivalent
- Over 20 min while awaiting result

Repeat twice or until 5 mmol/L increase in Na⁺

Follow-up management after 5 mmol/L rise Na⁺:
- Stop infusion hypertonic saline
- Keep IV line open minimum volume 0.9% saline
- Start diagnosis-specific treatment
- Limit increase Na⁺ to 10 mmol/L first 24 h
- Limit increase Na⁺ to additional 8 mmol/L every 24 h thereafter until Na⁺ 130 mmol/L
- Check Na⁺ 6 h, 12 h & daily until stable under stable treatment
General Management

Sodium change:

\[
\frac{\text{Na (infusate)} - \text{Na(serum)}}{\text{TBW} + 1}
\]

\[\text{TBW} = \text{Body weight} \times \%\text{Water}\]

\%\text{Water:}

- Elderly = 50%
- Adults = 55%
- Children = 60%

\[
\frac{513 \text{ mmol/L} - 105 \text{ mmol/L}}{80 \times 0.5 + 1}
\]

\[= 10 \text{ mmol/L change (if given 1L of 3%)}\]
SIADH

• Inappropriate secretion of ADH from posterior Pituitary or ectopic source

• Hyponatraemia with hypo-osmolality (<275mOsm/kg)

• Euvolaemia with raised urinary sodium (>20mOsm/kg) and inappropriately concentrated urine (>100mOsm/kg)

• Normal body response inhibited
  – Free water should be excreted
  – Normally urine osm should strictly be less than serum osm
SIADH – Normal physiology

Osmoreceptors detect high osmolality

ADH secreted

Aquaporin upregulated

Increased sodium reabsorption (Aldosterone)

Increased water reabsorption

Concentrated urine

Normalising Osmolality
Inappropriate ADH secretion

Collecting Duct

Increased water reabsorption

Low Plasma osmolality

Increased Luminal Sodium

High urine Na (>30)
High urine Osm (>100)
SIADH - Causes

• Intracranial pathology:
  – Trauma, Tumour, Infection, Thrombosis

• Pulmonary:
  – Small cell lung Ca, Mesothelioma, Abscesses, TB

• Malignancy:
  – GI (pancreas and stomach), Lymphoma, Leukaemia

• Drugs:
  – TCAs, SSRIs, AEDs, Vincristine, cyclophosphamide, Lithium, ecstasy

• Idiopathic
SIADH - Management

- If severe with symptoms
  - Treat with 3% saline until resolution of symptoms or Na-130mmol or increase of 10mmol/L

- Fluid restrict - 1st line (unlikely to cause adverse effects)

- NaCl tablets + low dose furosemide – 2nd line

- Oral urea (0.25-0.5g/Kg) – alternative 2nd line

- Demeclocycline, then Vaptans in resistant cases???

- Patients should not be given 0.9% saline
Hyponatraemia – When to refer/admit

• There are no unified UK guidelines
  – Only local guidelines and European guidelines

• NICE CKS indicate admission if patients:
  – Have acute onset or severe hyponatraemia (serum sodium concentration of less than 125 mmol/L)
  – Are symptomatic
  – Have signs of hypovolaemia

• Discussion with endocrinology if patient:
  – Has asymptomatic, moderate hyponatraemia (serum sodium concentration of 125–129 mmol/L).
  – If Addison's disease is suspected, admission or urgent referral may be required.
Hyponatraemia – When to refer/admit

• Refer to an endocrinologist, the urgency depending on clinical judgement:
  – If the cause of hyponatraemia is not clear.
  – If SIAD or another endocrine cause is suspected.
  – If reset osmostat syndrome or cerebral salt wasting is suspected.

• Refer to an appropriate specialist:
  – If the person has hyponatraemia thought to be caused by heart failure, kidney disease, or liver disease.
Summary

• Treatment of hyponatraemia depends on classification

• Ensure that hyponatraemia is a true hyponatraemia

• Treat the underlying cause where possible

• If euvolaemic, fluid restrict and complete sodium screen